## **REMARKS/ARGUMENTS**

Consideration of the above-identified application in view of the following remarks is requested. The claims pending and under consideration are claims 1-8.

## Claim Rejections - 35 USC § 103

1. In the Office Action, the Examiner maintained the rejection of claims 1-8 under 35 U.S.C. 103(a) "as being obvious over Meerpoel, WO 2002081460 A1 (cited on the IDS), in view of Daugan, WO 2003048121 (cited on the IDS), Daugan WO2000032582 (U.S. equivalent is 6,552,022), Dodic, WO2001096327 (cited on the IDS), Daugan WO2001097810 in further of Williams et al. "Novel Microsomal Triglyceride Transfer Protein Inhibitors" Expert Opinion On Therapeutic Patents 2003, 13, 479-488. In maintaining the rejection, the Examiner noted the following:

Applicant's representative has argued that the presence of an unsubstituted methylene group (CH<sub>2</sub>) is not taught by Meerpoel. The examiner respectfully disagrees as the whole teaching of Meerpoel must be considered as the compounds instant claims naturally read on the prior art genus. Meerpoel actually teaches a methylene, although no compounds with this pattern were actually made. A piecemeal analysis of Meerpoel is improper. Moreover the rejection was made in view of Daugan, WO 2003048121, Daugan WO2000032582 (U.S. equivalent is 6,552,022), Dodic, WO2001096327, Daugan WO2001097810 in further of Williams, which show that removal of the phenyl group in this position was well known and not essential to activity. . . .

This rejection is traversed. WO2002/081460 teaches compounds of general formula:

wherein Radical Z is defined as follows: Z is a bivalent radical of formula

Some examples of the bivalent radical Z of formula (a-5) would be (see bottom of page 4 to top of page 5 of WO2002/081460):

Further, in WO2002/081460, radical A is defined as: "A represents a bond, C<sub>1-6</sub>alkanediyl optionally substituted with one or two groups selected from aryl, heteroaryl and C<sub>3-6</sub>cycloalkyl;

<u>provided that when the bivalent radical Z is of formula (a-5) then A represents</u>

<u>C<sub>1-6</sub>alkanediyl substituted with one or two groups selected from aryl, heteroaryl and C<sub>3-6</sub>cycloalkyl" (*emphasis added*) (*See, e.g.,* page 5, lines 4-9).</u>

It is noted that it is correct that WO-2002/081460 also teaches that radical A can be unsubstituted methylene, but only for those compounds wherein radical Z is other than (a-5). WO-2002/081460 clearly teaches that when radical Z is of formula (a-5) then radical A <u>must</u> be substituted.

The Examiner may not simply pick and choose only those portions of the reference which support the Examiner's position. It is respectfully submitted that one of ordinary skill in the art in viewing WO2002/081460 as a whole would understand that although WO-2002/081460 teaches that for compounds wherein Z is other than a piperidinyl moiety, the radical A may be represented by unsubstituted piperidinyl, however, for compounds wherein Z is piperidinyl then radical A must be a substituted  $C_{1-6}$ alkanediyl.

WO2002/081460 fails to teach or suggest that when radical Z in the compounds of WO2002/081460 represents a piperidinyl group, then radical A may represent a methylene group which is unsubstituted. In fact the teaching in WO2002/081460 is exactly the opposite: when radical Z represents a piperidinyl group then radical A in the compounds of WO2002/081460 must be substituted. Thus one of ordinary skill in the art viewing the whole teachings of WO02/081460 would not be motivated to include an unsubstituted radical A when radical Z represents a piperidynyl group, as when radical Z represents a piperidinyl group then WO02/081460 indicates that radical A in the compounds of WO02/081460 must be substituted.

The Examiner again appears to rely on Examples in Daugan, WO 2003048121, Daugan, WO 2000032582, Dodic, WO2001096327, Daugan, WO 2001097810, and the discussion in the Williams reference that "removal of the phenyl group in this position was well know and not essential to activity."

It is respectfully submitted that claimed compounds of the present invention have the following general structure:

piperidinyl with ring nitrogen facing the biphenyl moiety

whereas the other citations raised by the Examiner include the following general structures:

WO-03/048121

$$R^{2}$$
 $N-R^{3}$ 
 $(I)$ 

WO-00/32582

$$\begin{array}{c|c}
R^2 \\
N-X \\
Z-R^1
\end{array}$$
(1)

WO-01/96327

WO-01/97810

It is respectfully submitted that the references (WO-03/048121, WO-00/32582, WO-01/96327, WO-01/97810) cited by the Examiner include either a piperazinyl moiety (two ring nitrogen atoms), or piperidinyl moiety wherein the ring nitrogen is

facing the oppositie side of the biphenyl moiety which would correspond to the biphenyl moiety of the claimed compounds of the present invention. It is respectfully submitted that WO-03/048121, WO-00/32582, WO-01/96327, WO-01/97810 fail to teach or suggest a compound wherein the piperidinyl moiety is facing with its ring nitrogen in the direction of the biphenyl part of its chemical structure as in the compounds claimed in the present invention.

Further, Williams et al., Expert Opin. Ther. Patents 13(4), 479 – 488 (2003) fails to teach or suggest compounds having a piperidinyl moiety wherein the ring nitrogen is facing the biphenyl portion of the chemical structure.

In view of the above, it is respectfully submitted that the skilled person would not be motivated to combine WO-03/048121, WO-00/32582, WO-01/96327, WO-01/97810, and Williams et al., Expert Opin. Ther. Patents 13(4), 479 – 488 (2003) with WO2002/081460.

Further, in view of WO-2002/081460 it is respectfully submitted that one of ordinary skill would understand that when compounds described therein having a piperidinyl moiety wherein the ring nitrogen is facing the biphenyl portion of the chemical structure, then radical A <u>must</u> be substituted.

Accordingly it is respectfully submitted that the compounds of the present invention include a unique structural element (e.g., a methylene group which is NOT substituted) that is not taught nor suggested by WO2002/081460 in view of Daugan, WO 2003048121 (cited on the IDS), Daugan WO2000032582 (U.S. equivalent is 6,552,022), Dodic, WO2001096327 (cited on the IDS), Daugan WO2001097810 in further of Williams et al. "Novel Microsomal Triglyceride Transfer Protein Inhibitors" Expert Opinion On Therapeutic Patents 2003, 13, 479-488.

In view of the above, the Examiner is respectfully requested to remove this rejection.

2. Claims 1-8 were again rejected under 35 U.S.C. 103(a) "as being obvious over Meerpoel USPG Pub 2006/0040989 in view Meerpoel, WO 2002081460 A1 (cited on the IDS) in further view of Williams et. al. 'Novel Microsomal Triglyceride

Transfer Protein Inhibitors' Expert Opinion on Therapeutic Patents 2003, 13, 479-488."

In response, the applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). As noted by the Examiner, this rejection might be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP §706.02(1)(1) and §706.02(1)(2).

It is respectfully submitted that the reference Meerpoel USPG Pub 2006/0040989 is disqualified under 35 U.S.C. 103(c) as prior art as the application and this reference were, at the time the invention was made, owned by, or subject to an obligation of assignment to, the same person.

In view of the above, the Examiner is respectfully requested to remove this rejection.

## Claim Rejections - Double Patenting

Claims 1-8 were again provisionally rejected on the ground of nonstatutory obviousness-type double patenting "as being unpatentable over claims 1-7 of copending Application No. 10/474,281 in view of Daugan, WO 2003048121 (cited on IDS), Daugan, WO 2000032582 (U.S. equivalent is 6,552,022), Dodic, WO 2001096327 (cited on IDS), Daugan, WO 2001297810 in further view of Williams et al. "Novel Microsomal Triglyceride Transfer Protein inhibitors" Expert Opinion On Therapeutic Patents 2003, 13, 479-488."

As this rejection is provisional, applicants will address such rejection upon indication by the Examiner that the claims are otherwise allowable.

Early favorable action on the merits is respectfully requested.

Please charge any fees, which may be required for this submission to Johnson & Johnson Deposit Account 10-0750/PRD2172USPCT/DK.

Respectfully submitted,

By: /David Knasiak/ David Knasiak Reg. No. 45,991

Johnson & Johnson One Johnson & Johnson Plaza New Brunswick, NJ 08933-7003 (732) 524-1522

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